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The Ongoing Study of The Chemistry of The Marine Inhabitants of The Ramsar Site of Port Royal, Jamaica

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ABSTRACT

Research efforts to examine the chemistry of marine organisms collected from the Ramsar site of Port Royal, Jamaica, has led to the isolation of a range of compounds as diverse as the species from which they were derived. Six sponges, two algal species, one ascidian and one soft coral collected from the mangrove area and the shallow coastal reefs were studied to yield compounds including steroids, aromatic compounds and terpenoids.

Indexing terms/Keywords: Port Royal, Mangrove, Reef, Marine, Chemistry

Subject Classification: Marine Chemistry

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INTRODUCTION

Situated at the entrance to the Kingston Harbour, Jamaica, the town of Port Royal lies at 17^{0}56′N 76°50′W and is the site of an old British naval station. With the dubious historical distinction of being the 'wickedest city', the earthquake of 1692 plunged two thirds of the city into the sea. Stretching from the Palisadoes to Port Royal, this unique Jamaican Ramsar site is home to an array of marine organisms, some of which inhabit the reefs and the open waters while others compete for space on heavily laden mangrove roots. Marine organisms in the Port Royal locale are sourced from a range of depths, habitats and microhabitats. The inhabitants of the environment include the full gamut of marine invertebrates including ascidians, barnacles, sponges, soft corals, crustaceans and algae which share the space with a wide variety of fishes and shelled organisms [1].

The fascination of the diversity of the marine invertebrates of Port Royal has led to the desire to investigate the chemistry of its sessile, soft bodied inhabitants whose defense weaponry to control or eliminate predation may have a chemical basis. The marine environment has served as a potent source of molecules with unique structural features and diverse applications [2-4].

Ascidians, otherwise known as tunicates or sea squirts, occur as solitary individuals or colonial species. These filter feeders ingest water from the surroundings, retain the useful nutrients and thereafter release the water through an exhalent siphon. One of the most abundant and well-researched significant organisms in the Ecteinascidia lagoon area of Port Royal is the orange ascidian *Ecteinascidia turbinata*. The chemistry of this ascidian species was extensively studied, resulting in the development of the commercially available drug Trabectidin, which was formulated with the compound ETC743 as the active component of the EU and FDA-approved drug [5]. It is important to note that secondary metabolites of ascidians are as diverse as the organisms themselves, ranging from alkaloids to terpenoids to macrolides [6-7].

A 2003 study of the ascidian population in the Port Royal region led to the identification of thirty nine ascidians from 23 genera. Commonly occurring species, many of which have been observed in recent years, include *Polyclinum constellatum, Trididemnum hians*, five *Didemnum* species, *Lissoclinum fragile, Diplosoma listerianum, Distaplia bermudensis* , two *Eudistoma* species, *Clavelina oblonga, Rhodosoma turcicum*, four *Perophora* species, three *Ecteinascidia* species, two *Ascidia* species, two *Phallusia* species, *Botrylloides nigrum* , two *Symplegma* species, *Polyandrocarpa tincta, Polycarpa spongiabilis*, two *Styela* species, *Herdmania momus, Pyura vittata*, two *Microcosmus* species and *Molgula occcidentalis* . As is common in other habitats around the world, the concentration and occurrence of these organisms vary over time, so the distribution of these ascidians today is impacted by changes in the chemistry of the water as well as predation and the introduction of invasive species, all of which impact the survival and viability of the species [8].

Sponges are sessile organisms which produce an expanse of secondary metabolites many of which have potential as therapeutic agents [9]. Other compounds are utilized for biomedical research purposes due to their ability to induce different disease conditions. These compounds include halichondrine A from *Halichondria okadai* which is a tumour promoter and a probe of cellular recognition [10]. One of the persistent challenges, however, in drug discovery efforts from marine sources relates to the supply of sufficient quantities of the bioactive compounds for commercial applications. While synthesis of the compound is an option, it may be a lengthy or expensive route as compared with the isolation procedure from its natural source. In recent years, it has been found that microbes associated with sponges function as the producers of some of these bioactive compounds [11-12]. Studies conducted by Hechtel in 1965 reported on the occurrence of 54 species of Port Royal sponges from 19 families, reporting on morphological details, field characteristics and spicule types from ten habitats [13].

In an evaluation of the mangroves along the Palisadoes strip, investigators Webber and Jackson examined nine sites with variations in depths, light intensity, total suspended solids and water currents. From this study, it was found that these factors affected the concentrations of the sponge species. The sponges thrived more in low light intensities, shallower depths and with fewer suspended solids. The sponges found on the prop roots of the Rhizophora mangle in the nine locations were several Haliclona species, Calyx podatypa, Amphimedon viridis, Niphates amorpha, N. erecta, Xestospongia muta, Mycale microsigmatosa, Tedania ignis, Lissodendoryx isodictyalis, Halichondria melanodocia, H. magniconulosa, Hymeniacidon heliophila and Terpios zeteki were identified. The commonly occurring species were M. microsigmatosa, T. zeteki and H. hogarthi [14].

Ranging in form from minute cells up to the large seaweeds of the Antarctic spanning many meters in length, algae are abundant species in the environment, producing a wide range of compounds including halogenated terpenoids, fatty acids and lipids [15]. They are a diverse group of non-flowering cellular plants comprising three main phyla; Chlorophyta (green algae), Phaeophyta (brown algae) and Rhodophyta (red algae). While microscopic species are the most commonly occurring algae, all algae are estimated to consist of over 72,000 species with names published for approximately 40,000 species [16]. These plants are limited in the depth at which they can survive because light penetration is essential for the photosynthetic process. Marine algae and sea grasses function as the primary producers, converting energy from the sun into carbohydrates which are subsequently utilized in some way by the majority of the other inhabitants of the sea including fishes and sea urchins who benefit directly by feeding on the plants. The increased concentration of algal species on the reefs throughout the Caribbean was due in large part to the mysterious die off of the herbivorous sea urchin Diadema antillarum in the 1980's. Recovery of the sea urchin has been slow, resulting in a concomitantly slow recovery of the health of the reefs across the Caribbean region [17].

The Port Royal coastal reefs have been observed to be home to a variety of algal species. In contrast, many macroalgal species are not observed on the prop roots in the mangrove area but species such as Caulerpa sertularioides have been observed at the edges of some of the lagoons in Port Royal.

Soft corals are abundant inhabitants of the reefs of the Caribbean, growing to several metres high in deeper waters. Comprehensive research work has been conducted on the extracts of these organisms in the Caribbean, yielding compounds with varying bioactivities [17]. Occupying shallow as well as deeper habitats in Port Royal, the identification of the species can sometimes be problematic due to the paucity of biologists who work with these organisms.

The chemistry of some of the invertebrates of these reef and mangrove habitats is currently under investigation and this report chronicles aspects of the work being conducted in this regard. The work being carried out on the Port Royal mangrove dwellers is documented below, while the isolates of the reef organisms are discussed in the subsequent section.

THE CHEMISTRY OF SELECTED INHABITANTS OF THE MANGROVES

The mangrove area of Port Royal is one of its most distinctive features and an extensive system of mangrove roots, Rhizopora mangle L., is found to the east of the town. The species peak density on these adventitious roots can be as high as 5000 organisms per m^2 [1]. The ecology of the habitat is such that, during very heavy periods of rain, there is a heavy influx of fresh water, leading to the death of many of the species. As such, the ecosystem is a dynamic one, with variable concentrations of the organisms throughout the year.

The objective of our study of the chemistry of the marine species from this Ramsar site is the isolation, characterization and biological evaluation of extracts and pure compounds in order to identify possible therapeutic or agricultural applications.

The organisms from the mangrove area which were studied were the ascidian Eudistoma olivaceum, the sponges Terpios zeteki and Tedania ignis and the alga Caulerpa racemosa, the chemistry of which will be discussed in this section.

Eudistoma olivaceum

Phylum: Eurochordata

Class: Ascidiacea

Order: Aplousobranchia

Family: Polycitoridae

Genus: Eudistoma

Species: E. olivaceum

Eudistoma olivaceum occurs as a yellowish-blue colony of tunicates. Collected at the Goodbody channel and Fort Rocky Lagoon at a depth of approximately 1-2 m, the sample was collected and frozen. The frozen sample was extracted with dichloromethane followed by methanol to yield lipophilic and methanolic extracts [19].

The lipophilic fraction was fractionated on a gravity silica column with gradient elution using mixtures of hexane, ethyl acetate and methanol to yield fourteen fractions. The fifth fraction was further subjected to gravity silica column with gradient elution using mixtures of hexane: acetone and methanol to yield six fractions, the second of which was subsequently purified by use of a gravity silica column with gradient elution using mixtures of hexane, acetone and methanol to yield a mixture of two isomers, eudistomins G **(1)** and H **(2)**. Eudistomin G was further purified as colourless needles [19].

The methanolic fraction was subjected to separation on Sephadex LH-20 in methanol, followed by fractionation on a gravity reversed phase silica column to yield eudistomins I **(3)** and P (**4**) [19]. A wide range of eudistomins have been isolated from

E. olivaceum species collected in other studies and bioactivity associated with these compounds includes antiviral and antimicrobial activity [20-21].

Tedania ignis

Phylum: Porifera

Class: Demospongiae

Order: Poecilosclerida

Family: Myxillidae

Genus: *Tedania*

Species:*T. ignis*

This bright orange sponge is a highly prominent inhabitant of the mangrove, especially nearby the Port Royal Lagoon where the mangrove roots are laden with the organism. Known as the Fire sponge, contact with this species in the water can cause dermatitis [22]. This sponge is thought to have a mechanical defense system which prevents predation by fishes and other sea creatures.

T. ignis was collected, cleaned of epibionts, extracted with organic solvent and the resultant orange gum was procured upon rotary evaporation of the extract. From the preliminary evaluation of the fractions and pure compounds obtained from column chromatography, the lipids β-sitosterol, phytol and batyl alcohol were identified along with a ceramide [23]. Further investigations of fractions identified by ^{1}H NMR analysis containing aromatic signals will be conducted to determine the structures of additional compounds biosynthesised by this sponge.

Bermudan specimens of *T. ignis* led to the identification of several aromatic secondary metabolites while collections of the sponge from Summerland Key, Florida, resulted in the isolation of small quantities of tedanolide, a macrolide found to exhibit potent bioactivity against cancer cell lines [24]. Tedanolide has been the subject of synthesis due to its potent activity against lymphatic leukemia, found to increase the lifespan of infected mice by 23% [25]. Due to the paucity of the yield of this compound, it is surmised that the compound may be produced by microorganisms living in the sponge [24].

Terpios zeteki

Phylum: Porifera

Class: Demospongiae

Order: Hadromerida

Family: Suberitidia

Genus: *Terpios*

Species:*T. zeteki*

Growing abundantly on the mangrove roots throughout Port Royal and on ropes and columns suspended in the water, the most striking feature of this sponge species is that they occur in a range of colour morphs, from yellow, yellowish-green, to orange, red, purplish-pink and dark green.

In our study, *Terpios zeteki* was collected from the Port Royal mangroves, cleaned of extraneous matter, frozen and then exhaustively extracted in a 1:1 methylene chloride: methanol solvent mixture to afford a crude extract which was obtained after rotary evaporation. Fractionation via vacuum liquid chromatography and subsequent normal phase HPLC using 10% isopropanol: hexane afforded a steroidal mixture which was further purified by yield the C27 steroid cholestanol (5α-cholestan-3β-ol) **(5)** [19].

Preliminary investigation of three of the colour morphs of *T. zeteki* revealed that the chemical profiles of the lipid extracts did not differ significantly. Their aqueous extracts reflected the colours of the sponges, suggesting that polar pigments provided the different colours [26]. The occurrence of the range of colours of the sponges occupying the same geographical space remains a puzzling phenomenon.

Terpios zeteki was one of the first marine sponges to be investigated by Bergmann and coworkers in 1949. Obtained from Hawaii, the acetone extract yielded cholestanol and neospongosterol [27]. Further research work executed on the Hawaiian-sourced organism in 1979 led to the isolation of the steroids including 5α-stanols and traces of 5α-24-norcholestan-3β-ol. Other minor sterols were also detected in that study [28].

The compound 5α-cholestan-3β-ol is thought to induce apoptosis of cornea endothelial cells as well as cerebellar neuronal cells in vitro [29].

Caulerpa racemosa

Kingdom: Plantae

Division: Chlorophyta

Class: Bryopsidophyceae

Order: Bryopsidales

Family: Caulerpaceae

Genus: *Caulerpa*

Species: *C. racemosa*

Caulerpa racemosa, a common green algae, otherwise known as sea grapes, is eaten in some Pacific cultures due to the fact that it is rich in folic acid, vitamins A, B1 and C and is also reported to reduce high blood pressure [30]. In our study, the crude extract of the green algae *Caulerpa racemosa* displayed greater than 70% inhibition (74-98%) with three cancer cell lines at 10 µg/ ml [31]. The Jamaican *C. racemosa* has been found to contain caulerpin **(6)** and caulerpinic acid **(7)**, constituents similar to that which have been found by other researchers. [32-33]

In a study by Nagaraj and coworkers, the methanolic extract has been found to display larvicidal activity while in another study, aqueous extracts of the algae have been found to have potential applications in the preparation of very stable nanoparticles of silver, thereby suggesting possible applications of this species [34-35].

THE CHEMISTRY OF SELECTED INHABITANTS OF THE REEF

Our continuing investigation of sponges dwelling on the reef in the vicinity of Port Royal, many of which are thought to manufacture bioactive compounds as chemical defenses against predators, led to the organic extraction of the Verongid sponge *Aplysina fistularis*, the erect red *Amphimedon compressa,* the army green *Halichondria melanodocia* and the zooid-associated *Iotrochota birotulata.* Other species being studied include the gorgonian *Plexaurella nutans* and the algal species *Canistrocarpus cervicornis*.

Aplysina fistularis

Phylum: Porifera

Class: Demospongiae

Order: Verongida

Family: Aplysinidae

Genus: *Aplysina*

Species: *A. fistularis*

Verongid sponges have been extensively examined and found to contain a variety of compounds, many of which display bioactivity. The chemistry of several members of the *Aplysina* genus has been investigated with brominated alkaloids being the most prominent class of compounds identified, including the aerothionins [36] and the related fistularins.

An examination the metabolite profile of the Jamaican *A. fistularis*, collected from Drunken Man's Cay in Port Royal, showed that the brominated isoxazoline compounds aerothionin **(8)** and 11-oxoaerothionin **(9)** were present [37].

11-Oxoaerothionin has been found to be cytotoxic towards several cancer cell lines, including T-cell leukemia, human colon (HCT 116) cell lines and melanoma (SK5-MEL). This compound was also found to inhibit the growth of several bacterial strains including *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* in antimicrobial assays [38].

Iotrochota birotulata

Phylum: Porifera

Class: Demospongiae

Order: Poecilosclerida

Family: Iotrochotidae

Genus: *Iotrochota*

Species: *I. birotulata*

The sponge *Iotrochota birotulata* was collected by SCUBA diving off the Port Royal coastline. Commonly referred to as the green finger sponge, it occurs as thick branches (1.5 cm diameter). Purplish- black or green in colour, the organism is usually colonised by abundant golden zooanthids. The sponge was carefully cleaned of all extraneous debris, cut up, frozen and lyophilized. Extraction was effected using *n*-hexane, methylene chloride and methanol. Extracts were concentrated using a rotary evaporator to yield crude residues. When the crude extracts of the sponge were tested against the sweet potato weevil *Cylas formicarius elegantulus*, 100% mortality was observed at a concentration of 2 µg/mL after 72 hours [39].

A portion of the hexane extract was purified on a silica gel column and the fraction eluting in 10% methylene chloride: hexane contained a bright red-orange solid which was purified using 5% methylene chloride: hexane to obtain the carotenoid derivative renierapurpurin **(10)**. A white solid identified to be β- sitosterol was also obtained from the hexane extract.

The methylene chloride extract was subjected to repeated flash silica gel column chromatography to afford the tyrosine derivative 1,3-dibromo-5-{2-[(*p*-hydroxyphenyl)-acetamido]ethyl}-2-[3-(-methyl-2-butenamido)-propoxy] benzene **(11)** [39].

The *Iotrochota* genus has been shown to possess a variety of secondary metabolites, including alkaloids, sphingolipids , bromoindole and tyrosine derivatives [40-41]. A few of isolates exhibit cytotoxic and anti-inflammatory activity as well as antibacterial activity. Records have shown that the methanol/water extracts significantly inhibited larval attachment at 0.1 mg mL^{-1} and are considered as possessing anti-settlement activity [42].

Amphimedon compressa

Phylum: Porifera

Class: Demospongiae

Order: Haplosclerida

Family: Chalinidae

Genus: *Amphimedon*

Species: *A. compressa*

This prominent maroon-red sponge occurs commonly in the Port Royal reef waters and resembles a rope-like, usually branched structure with a smooth, porous surface. Samples were collected by SCUBA divingoff the Port Royal coast at a depth of 8 m. Upon collection, freeze drying and extraction with methanol: methylene chloride (1:1), a maroon coloured gum was obtained, which, when subjected to size exclusion chromatographic separation on Sephadex LH-20 afforded eighteen fractions. The first two fractions were intense red-brown in colour while fractions three and four were light red-brown, exhibiting UV absorption maxima at 268 nm. ^{1}H NMR analysis of these fractions revealed that they contained similar resonances in both the aromatic and aliphatic regions. The main constituent of the extract was found to be the bioactive polymeric red compound amphitoxin **(12)**, which exhibited toxicity to the moon fish *Xiphophorus variatus* [43]. Fractions containing the amphitoxin which were subjected to cytotoxicity testing were found to be bioactive against selected cancer cells. Currently, chemical modifications of this compound are underway to evaluate the degree of importance that elements within the amphitoxin structural unit have to the retention of its bioactivity.

Halicondria melanodocia

Phylum: Porifera

Class: Demospongiae

Order: Halichondrida

Family: Halichondriidae

Genus: *Halichondria*

Species: *H. melanodocia*

The *Halichondria* genus consists of over 60 species and, over the years, novel and bioactive metabolites of varying structural classes and pharmacological activities have been isolated from this genus. Structural classes range from macrolides, sequiterpenes, polyethers, alkaloids and sterols with a dominance in anti-tumour activities [44-45].

Halichondria melanodocia was collected in the Port Royal vicinity at a depth of approximately 1 m. This sponge was dark-grey in appearance in the water and a dark dull green colour when taken out of the water. It had a soft texture with visible oscules ranging from 1-3 cm in diameter, protruding from the surface. The crude extract of this sponge exhibited moderate activity against the insect pest, *Cylas formicarius* (the sweet potato weevil) with 60% mortality occurring after 72 hours at a concentration of 6 micrograms. The sponge was collected, frozen and lyophilized to give a dry weight of 276 g. The sample was extracted twice in dichloromethane after which it was steeped in methanol. This extraction yielded 6.8 g of lipophilic extract and 45 g of the methanolic extract. The latter fraction was first dissolved on methanol and the methanol soluble portion was placed in a methanol Sephadex LH-20 column to yield eight fractions. Fraction four was subjected to further purification and subsequent ^{1}H, ^{13}C and 2D NMR data analysis to afford two nucleosides **(13)** and **(14)**. The common epidioxysteroid **(15)** was also isolated from *H. melanodocia* [19].

Plexaurella nutans

Phylum: Cnidaria

Class: Anthozoa

Subclass: Octocorallia

Order: Alcyonacea

Suborder: Holaxonia

Family: Plexauridae

Genus: *Plexaurella*

Species: *P. nutans*

Belonging to the Phylum Cnidaria which is one of the major phyla of the subkingdom Metazoa, gorgonians of the class Anthozoa also include sea anemones, hard and soft corals and sea pens. These organisms all contain a sac-like body with an opening that functions as the mouth and anus. Most of the metabolites reported from Cnidaria are from the class Anthozoa and terpenes are the common constituents [46]. Detailed work was conducted on the gorgonian *Plexaurella nutans.*

The sample was collected from Lime Cay, Port Royal at a depth of 14 m. Known locally as the giant slit pore sea rod, there is a tendency for divers to avoid contact with the organism due to the itching that results from this contact. The octocoral was air dried, stripped and extracted twice with CH_2Cl_2 followed by methanol to yield brown oily gums. A portion of the dichloromethane extract was subjected to vacuum liquid chromatography on silica gel with increasing proportions of CH_2Cl_2 in hexanes, with final elution in a methanol: dichloromethane mixture. Further purification of the non-polar oily fraction obtained from the vacuum liquid chromatography and analysis by GCMS led to the identification of the terpenes curcumene **(16)**, β-bisabolene **(17)** and santalene **(18)**.

Previous investigations of *P. nutans* from an undetermined Caribbean location afforded the sesquiterpene hydrocarbons (+)-β-bisabolene, (-)-α-curcumene and (-)-β-curcumene which have been reportedly isolated from another West Indian gorgonian, *Muricea elongata* [47].

Canistrocarpus cervicornis

Kingdom: Chromista
Phylum: Ochrophyta
Class: Phaeophyceae
Subclass: Dictyotophycidae
Order: Dictyotales
Family: Dictyotaceae
Tribe: Dictyoteae
Genus: *Canistrocarpus*

Species: *C. cervicornis*

Specimens of *C. cervicornis* were collected by SCUBA diving at Drunken Man's Cay, air-dried and exhaustively extracted with hexane, methylene chloride, ethyl acetate, and methanol. The methylene chloride extract was subjected to flash silica gel column chromatography to afford twelve main fractions. Fraction 8 was further purified to yield the new dolastane diterpene 4*R*-acetoxy-8*S*,9*S*-epoxy-14*S*-hydroxy-7-oxodolastane (**19**) as a colourless gum. Fraction 11 was crystallized in methylene chloride to yield white orthorhombic crystals of (4*R*,9*S*,14*S*)-4,9,14-trihydroxydolast-1(15),7-diene **(20)** while fraction 12 was further fractionated on silica gel to yield 4*R*-hydroxy-8*S*,9*S*-epoxy-14*S*-hydroxy-7-oxodolastane (**21**). Moderate, concentration-dependent cytotoxicity against human tumour cell lines PC3 and HT29 was observed with the compounds isolated [48]. Work conducted on the Brazilian *C. cervicornis* led to the isolation of a dolastane exhibiting antileishmanial activity [49], thereby confirming the diverse utility of compounds from marine sources.

Conclusions

The research work on organisms in the Port Royal area continues as we race against time to unlock the ocean's treasures before the populations become extinct. Currently, work is underway with the ascidians *Botrylloides perspicuum*, *Ascidia curvata* and *Clavelina picta* as well as the brown alga *Gracillaria mammilaris* as we continue to seek applications for our natural resources.

The plethora of organisms representing outstanding diversity in the Port Royal locale will undoubtedly continue to be a source of compounds of an equally structurally diverse nature. Consequently, the work to unlock the secrets of nature continues.

Conflicts of Interest

The author declares that no conflict of interest exists no conflicts exist, the authors should state this. Submitting authors are responsible for co-authors declaring their interests.

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